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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
COUNTS, GARY W

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,192	DELMAS ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- Th MAILING DATE of this communication appears on the cover sh et with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *3-9,12,22,28,31 and 2325* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,10,11,13-21,24,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 1 containing claims 1, 2, 10, 11, 13-21, 24, 29 and 30 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that Claims 1 and 3-9 each recite bringing a biological sample from an individual into contact, in vitro, with a means for measuring a specific marker of synovial disease, and determining the level of the marker and that it would appear that the searches for Groups I-VI would be fairly co-extensive. This is not found persuasive because of reasons set forth in the previous office action. Furthermore, as disclosed by Applicant on page 6 in the specification a synovial disease means an increase in turn-over, proliferation, degradation, inflammation, destruction, decomposition, pathological remodeling or degradation of the synovia or synovial collagen and an osteoarticular disease means a disease of one or more joints or which involves proliferation of the synovia and cartilage attack. Even though the method steps are roughly similar a method of diagnosing a synovial disease would be inherently different from diagnosing an osteoarticular disease each of the diseases may have different processes and thus would have different processes in methods. Further, the literature search for each method listed in Groups I-VIII would require different search terms and a different search strategy, which creates a burden on the examiner. While searches would be expected to overlap, there is no reason to expect the searches to be coextensive. The requirement is still deemed proper and is therefore made FINAL.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on 07/01/99. It is noted, however, that applicant has not filed a certified copy of the France 9908502 application as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2, 10, 11, 13-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it recites a method for diagnosing or monitoring the evolution of a synovial disease. It is unclear which is being done. Further, diagnosing would involve a definitive yes or no for having the disease, whereas monitoring would involve determining a progression. Therefore it is unclear how both are performed.

Claim 1 is vague and indefinite because it is unclear what markers are specific for synovail disease. The specification on page 2 discloses the specific marker for synovial disease is glycosylated pyridinoline, more particularly diglycosylated pyridinoline. It is recommended to incorporate the specific marker as taught in the specification into the claim.

Claim 1, part (iii) the recitation "optionally" is not a positive recitation and renders the claim indefinite. Furthermore, it is unclear how the diagnosis or monitoring of the synovial disease could be performed without step (iii). Without comparing the level of step (ii) with a reference or control. It would be unclear if an increased level is indicative of synovial disease or if a decreased level is indicative of synovial disease.

Claim 2 is vague and indefinite because it is unclear what applicant is trying to encompass. The claim appears to cover all individuals those having synovial disease and those susceptible of developing synovial disease. It is also unclear what makes a person susceptible of developing synovial disease (i.e. age, sex, exposure to a particular chemical or substance etc....).

Claim 13, the recitation "the destructive or non-destructive stage" there is insufficient antecedent basis for this limitation.

Claim 16 is vague and indefinite because of the use of an acronym (HPLC). Although the term may have art-recognized meanings, it is unclear if applicant intends to claim the prior art definitions. The term should be defined in its first instance.

Claim 17 is vague and indefinite because it is unclear if the recitations contained within parenthesis () are part of the claim or not.

Claim 17 is vague and indefinite because it is unclear what structural or functional relationship exits between the specific marker and creatinin. There is no guidance provided in the specification.

Claim 20 the recitation "the level of which alone" is vague and indefinite. It is unclear what applicant is trying to encompass. Also, does this mean that there are a

battery of markers and only the specific marker is elevated or is the specific marker compared to a control or does the mere presence of the marker indicate the degree of synovial tissue degradation.

Claim 20, line 2 "the degree of synovial tissue degradation" there is insufficient antecedent basis for this limitation.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 2, 16, 18 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Blum et al (Detectable levels of pyridinoline are present in synovial fluid from various patients with knee effusion: preliminary results European Journal of Clinical Investigation (1995) Vol 25, No. 6, pp. 438-441).

Blum et al disclose a method for early diagnosis of inflammatory joint diseases (synovial disease) such as rheumatoid arthritis and degenerative joint diseases such as osteoarthritis. Blum et al disclose measuring pyridinoline (marker). Blum et al disclose that pyridinoline is issued from the degradation of mature collagens in synovial tissue (p. 438). Blum et al disclose that the measurement is performed by high performance liquid chromatography (HPLC). Blum et al also disclose comparing the levels of pyridinoline with a knee effusion with post-traumatic effusion.

7. Claims 1, 2, 14, 15, 18 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Price et al (WO 95/02188).

Price et al disclose a method for diagnosing or tracking the progress of joint diseases (synovial disease) such as Rheumatoid Arthritis. Price et al disclose detecting YKL-40 (specific marker for joint disease) in a biological sample (page 5). Price et al also disclose that diagnosis of disease based on measured levels of YKL-40 can be made by comparison to levels measured in a disease-free control group or background levels measured in a particular patient (p. 13). Price et al disclose detecting YKL-40 by using a radioimmunoassay technique (p. 20).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 10, 11, 13, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blum et al in view of Robins et al (WO 89/12824).

See above for teachings of Blum et al.

Blum et al differ from the instant invention in failing to teach the specific marker is glycosylated pyridinoline or diglycosylated pyridinoline.

Robins et al disclose the measurement of glycosylated pyridinoline and diglycosylated pryidinoline which have been shown to be present in creased amounts in

various bone disorders and in arthritic disease (p. 4-6). Robins et al disclose that these markers are specific to a particular tissue of origin.

It would have been obvious to one of ordinary skill in the art to incorporate glycosylated pyridinole or diglycosylated pyridinole as taught by Robins et al as the markers for the method of Blum et al because Robins et al shows that the use of glycosylated pyridinole or diglycosylated pyridinole provides markers that are specific to a particular tissue of origin.

10. Claims 20, 24 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blum et al in view of Robins et al as applied to claims 1, 2, 10, 11,13-16 and 18-21 above, and further in view of Boguslaski et al (US 5,420,016).

See above for teachings of Blum et al and Price et al.

Blum et al and Robins et al differ from the instant invention in failing to teach packaging the components into a kit.

Boguslaski et al disclose assembling various system components into a test kit. By assembling these components into test kits, it makes it more convenient and facile for the test operator (col 7, lines 8-11).

It would have been obvious to one of ordinary skill in the art to package the reagents and components as taught by Blum et al and Robins et al into a kit because Boguslaski et al teaches that assembling components into test kits, it makes it more convenient and facile for the test operator.

Conclusion

11. No claims are allowed.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

St. Clair et al. (A cross sectional analysis of 5 different markers of collagen degradation in rheumatoid arthritis, Journal of Rheumatology (1998), 25 (8), 1472-1479). St. Clair et al disclose immunoassay for detecting pyridinoline.

Robins et al (US 5,283,187) disclose a method of monitoring collagen degradation comprising assaying a biological fluid for hydroxylysyl pyridinoline.

Kung et al (US 5,736,344) disclose serum pyridinium crosslinks assays.

Black et al (Urinary excretion of the hydroxypyridinium cross links of collagen in patients with rheumatoid arthritis, Annals of the rheumatic diseases 1989; 48: 641-644. Black et al disclose that higher concentrations of urinary pyridinoline in patients with RA and are associated with the activity of the disease.

Otsuka et al (Evaluation of Urinary Pyridinoline in healthy Adults and Patients with RA by and Improved HPLC Assay, Journ. Nutr. Sci. Vitaminol., 42, 485-490, 1996). Otsuka et al disclose a modified method for the determination of pyridinoline using HPLC.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for

the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary Counts

Gary W. Counts
Examiner
Art Unit 1641
May 15, 2003

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SUPERVISORY PATENT EXAMINER
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07/28/03